Asthma research at EPA's Nat'l Health & Environmental Effects Research Lab:

ENVIRONMENTAL RISK FACTORS FOR ASTHMA

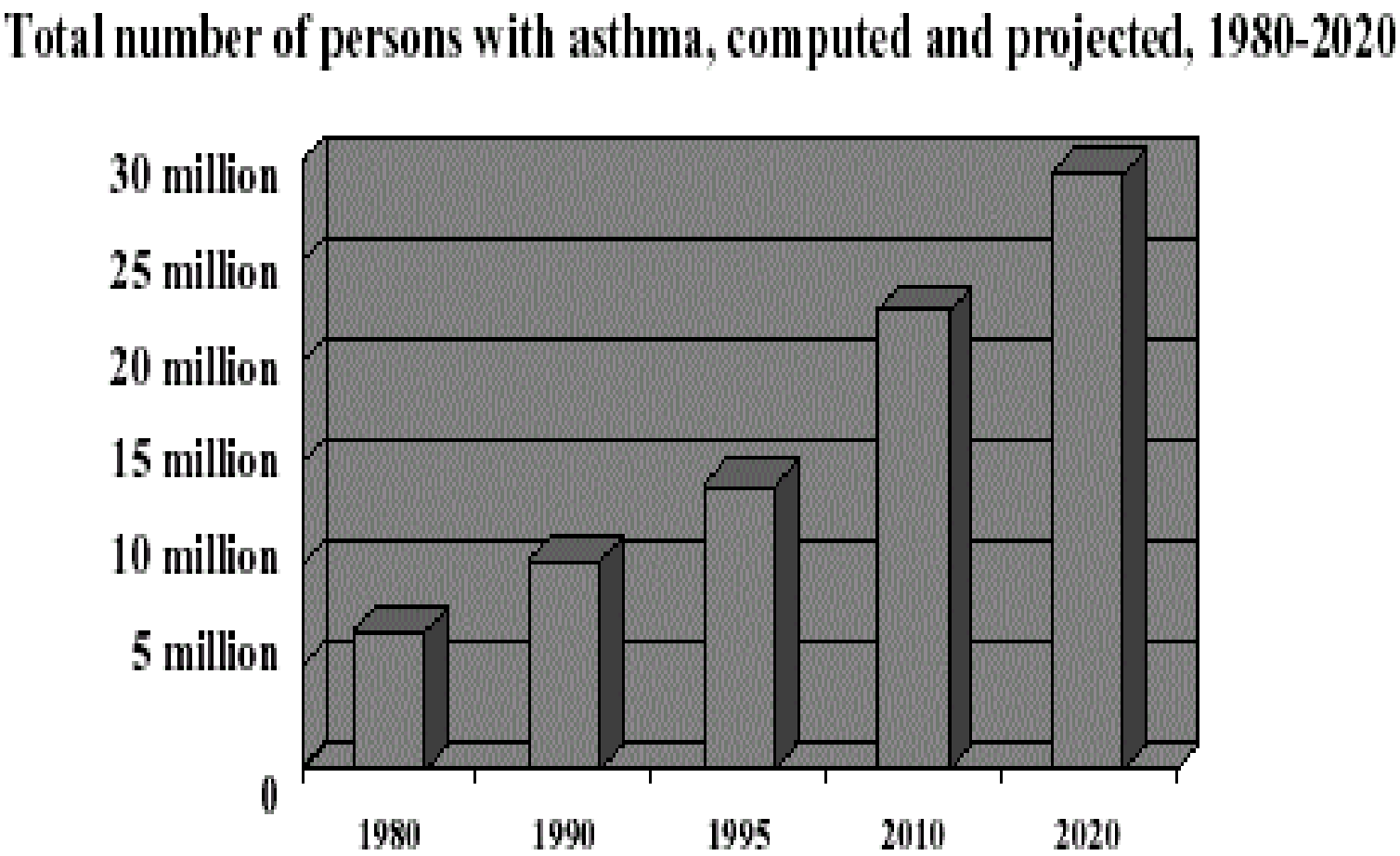
MaryJane K Selgrade

Experimental Toxicology Div., Nat'l Health & Environmental Research Laboratory, Office of Research & Development, U.S. EPA, Research Triangle Park, NC

Where is this talk going?

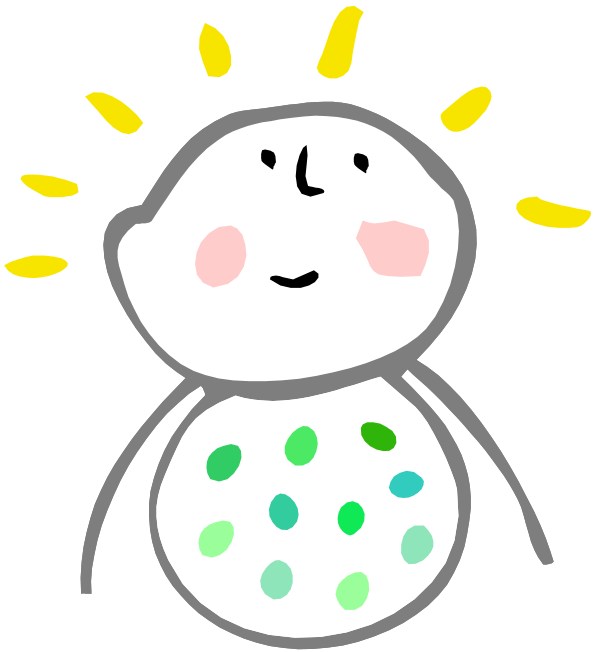
- **Why are we concerned about environmental influences on asthma?**
- **What exactly is asthma?**
- **What research is EPA's Office of Research and Development (NHEERL) doing in the area of asthma?**
- **What contributes to cumulative risk?**

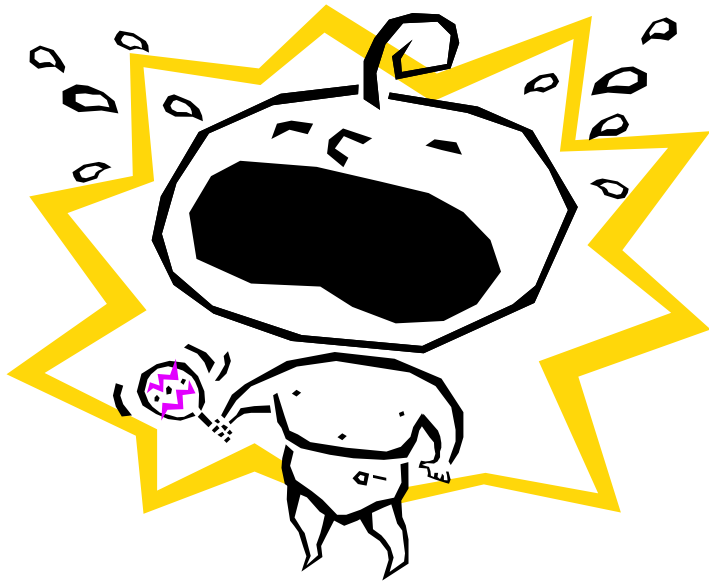
Increasing Prevalence of Asthma



Pew Environmental Health Commission, Johns Hopkins School of Public Health, May, 2000

Two Stages





Induction
Sensitization
(1st exposure)

Elicitation
Challenge
(subsequent exposure)

Characteristics of Allergic Asthma

- **Immediate Response**
  - Broncho-constriction
  - IgE mediated (IL-4)
- **Late phase**
  - Hyperresponsive to non-specific stimuli (methacholine)
  - Eosinophilic Inflammation
  - Th2 mediated (IL-5, IL-13)

ORD Asthma Research Strategy*

Research Areas

- **Induction & exacerbation of asthma**
  - ***Combustion-Related Products**
  - ***Bioaerosols**
  - **Air Toxics**
  - **Pesticides**
- **Susceptibility factor contributing to asthma**
- **Risk assessment**

***http://www.epa.gov/ord/htm/researchstrategies.htm#rs02**

NHEERL RESEARCH THEMES

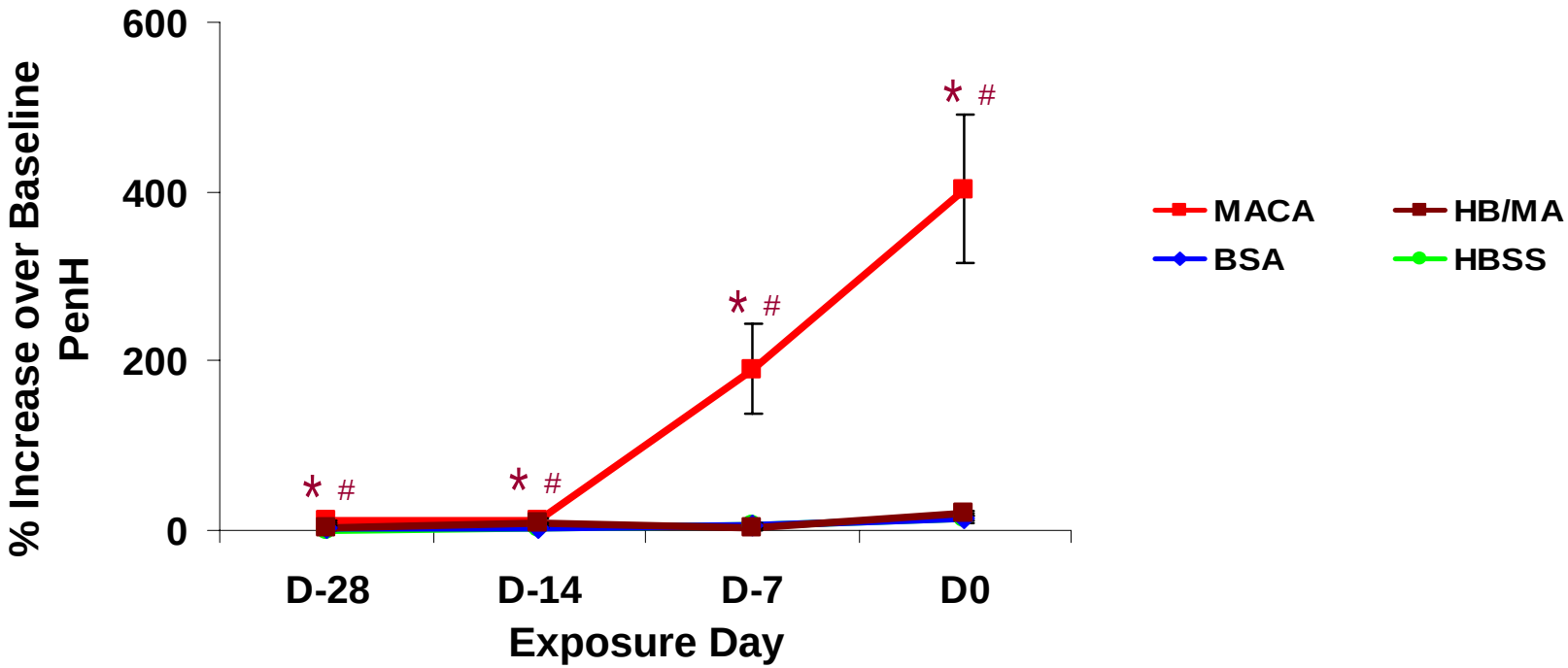
- **Identify and rank mold allergens which may be important in the induction of allergic asthma.**
- **Assess the effect of air pollutant exposure on the induction of asthma.**
- **Assess the effect of air pollutant exposure exacerbation phases of asthma.**

Mold contaminated wall board

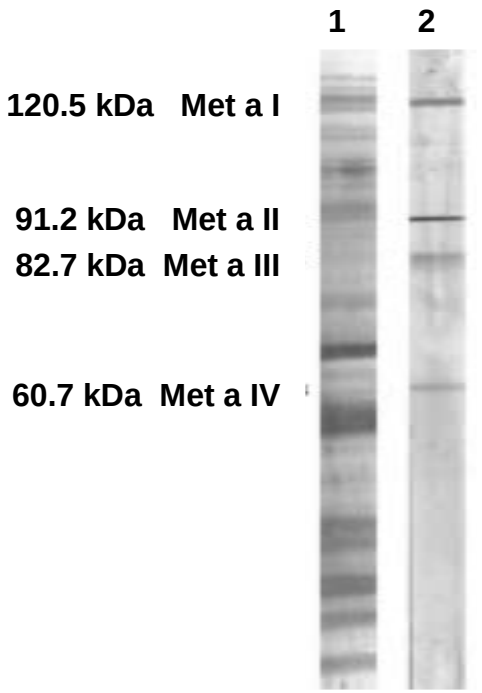
Cross Laboratory Project

- **Assess molds for potential & potency as asthmagens using an animal model**
  - ***Metarhizium anisopliae* (MACA) – a biopesticide**
  - ***Stachybotrys chartarum* (SCE-1) – water damaged building contaminant**
  - ***Penicillium chrysogenum* (PCE) – a common indoor mold**
- **Develop exposure assessment tools**
- **Develop methods to prevent or mitigate mold growth**

Multiple Exposures to Mold Resulted in Increased Immediate Respiratory Responses to Aspirated Mold Extract

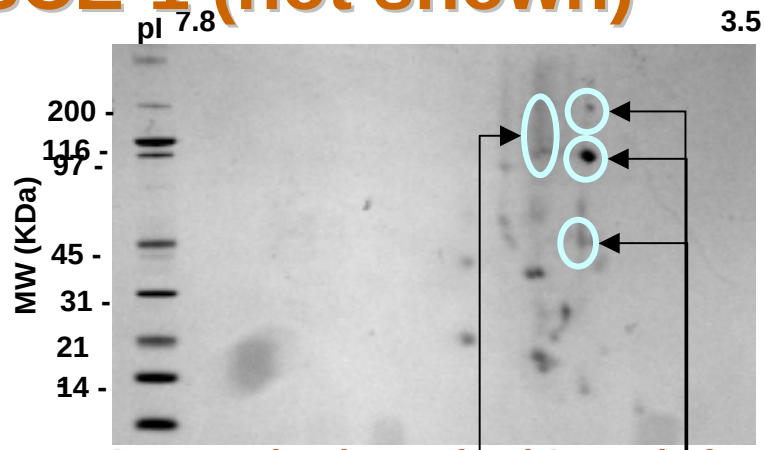


Several IgE Inducing Proteins Have Been Identified in MACA and SCE-1 (not shown)

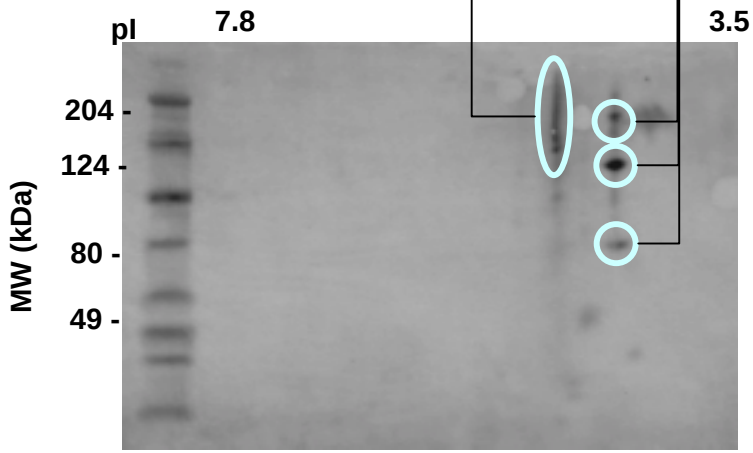


1. India Ink stain
2. Western Blot

Western Blot analysis using hyper-immune serum against MACA as the primary antibody, identified only 4 proteins that induce IgE. This data suggests only a few proteins in MACA are allergens.



Coomassie Blue stained 2-D gel of mycelium extract



2-D gel Western blot analysis of the mycelium extract using the hyperimmune serum confirms an IgE inducing protein(s) in the acidic range with high molecular weight

Fine Particles Can Be Emitted Directly or Formed in the Air from Gases

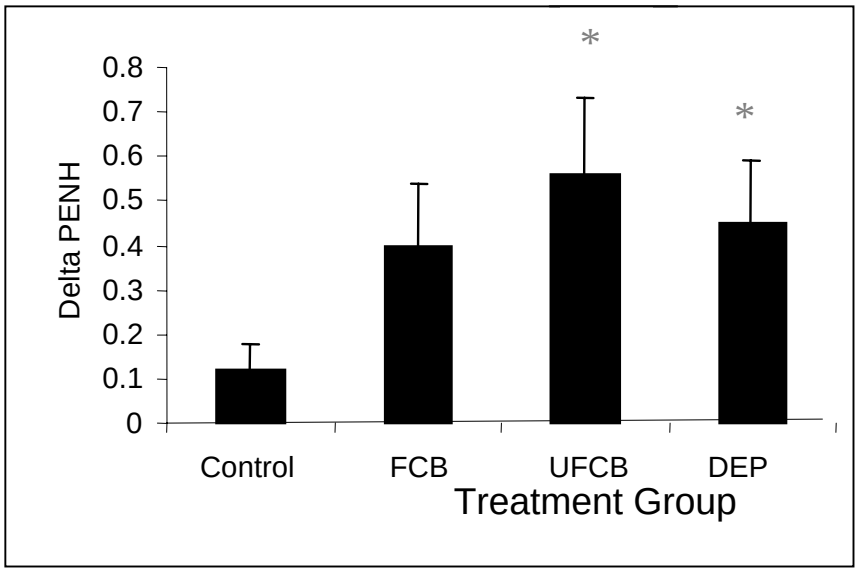
SPECIFIC AIMS

Develop assays to predict the ability of pollutants to enhance the induction or exacerbate the severity of allergic asthma

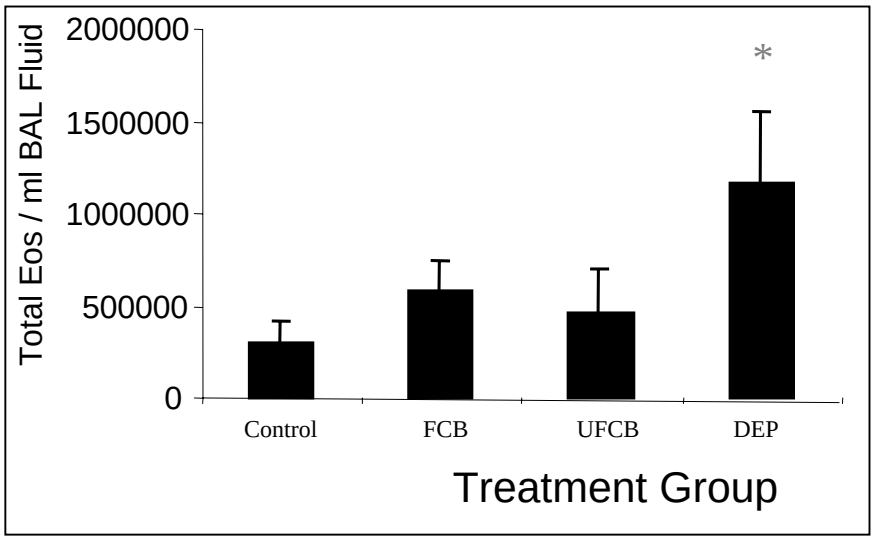
Test this approach using a prototypic pollutant (diesel exhaust) in *in vivo, in vitro* (animal and human studies) and in epidemiological surveys.

Use this paradigm to test the relative potency of different air pollution components

Adjuvant Effects of Carbonaceous Particles and Diesel



Pre-Exposure to CB and DEP Increases Immediate Airway Responses to HDM

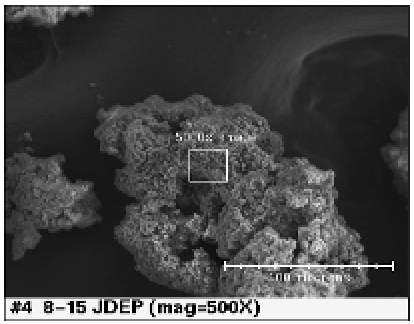


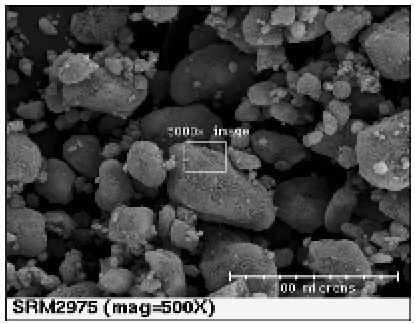
Pre-Exposure to DEP Increases Eosinophilia After HDM Challenge

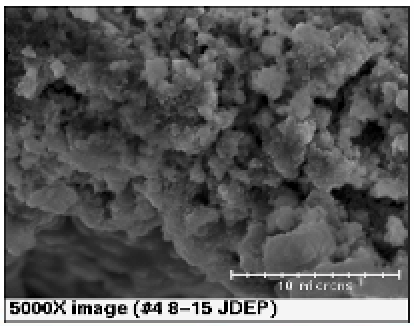
Singh et al, In Prep

All diesel samples are not created equally!

Physicochemical Comparison of A-DEP and NIST SRM DEP



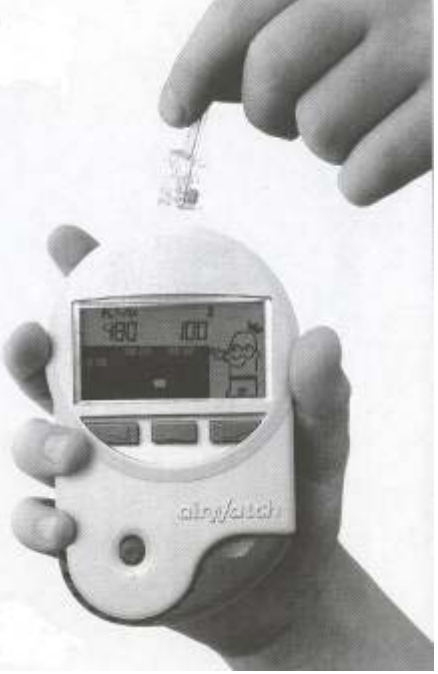




Carbon Analyses	A-DEP	SRM-DEP
Total Carbon (%)	60%	65%
Elemental Carbon (%)	9%	60%
Organic Carbon (%)	51%	5%

Singh et al, DeMarini et al, EHP June 2004


Bay
8



PACES I

- Population: <u>persistent</u> asthmatics, 8-18 years old, from Chapel Hill area
- Sample size: 28, rolling enrollment, 1-3 children/week, 9/2003-5/2004
- Clinical visits: 1 clinical evaluation (2-3 hr), 1 panel enrollment (45 min.), and 1 completion (10 min.)
- Epidemiological Panel (6 weeks)
  - Outcomes measured daily
    - electronic peak flow meter (2x daily, data sent 1x by modem)
    - internet daily health diary (1x daily)
  - Exposures: PM_{fine} & PM_{coarse}
    - Daily central site (HSD)
    - Home outdoor: for 1 week only

AAES I

- Population: persistent asthmatics, 18-50 years old, Chapel Hill area
- Sample size: 12, rolling enrollment, 1 adult/every other week, 9/2003-6/2004
- Epidemiological Panel (6 weeks)
  - Same as PACES I but with additional clinical visits & monitoring
    - 1 pre-study screening (1 hr)
    - Week 1: 5 daily clinical evaluations (2-3 hr)
    - 5 follow-up evaluations (1x week for next 5 wks.)
    - Week 1: Personal Daily PM_{fine} & PM_{coarse}

Cumulative Risks

- **Genetics**
- **Ages**
- **Environment**
  - **Ambient air pollutants**
  - **Biologics**
- **Lifestyle**